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Aerosol Therapy in Bronchopulmonary Disease

A Critical Evaluation

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• **Aerosol therapy has three principal objectives: Mobilization of bronchial secretions, relief of bronchospasm and topical chemotherapy. It has become an important tool in the treatment of bronchopulmonary diseases. The equipment for inhalation therapy, however, should be adequate. Both large-capacity and small-capacity nebulizers must be available, and they must be the kind that will produce a mist with most of its particles only 0.5 to 2.5 micra in diameter. These nebulizers may be used alone or in conjunction with a variety of appliances that will deliver the aerosols to the respiratory tract. The use of humidifying agents as aerosols is extremely helpful in patients with retained bronchopulmonary secretions. In some patients who have particularly thick or gelatinous secretions and in patients with mucoviscidosis, ordinary water or saline solution is often not enough. Hypertonic saline may be of value in these cases, and it is suggested that half-molar (2.9 per cent) saline be administered in 10 per cent propylene glycol. In these cases, preparations containing detergents (tyloxypal) or other preparations containing enzymes (desoxyribonuclease or trypsin) may be given by the aerosol technique, with care not to cause irritation.**

The bronchodilator aerosol agents are of proved benefit in the treatment of bronchospastic disorders and are indicated in most cases of asthma and in those cases of emphysema in which there is definite evidence of associated bronchospasm.

The value of the aerosol method of administering chemotherapeutic and antibiotic drugs has probably been overrated, and it is suspected that much of the benefit previously attributed to the therapeutic agent was actually a result of humidification and liquefaction.

TREATMENT BY INHALATION has been used in one form or another for many years. Long ago patients with asthma found that they might obtain temporary relief of bronchospasm by breathing the smoke of burning stramonium leaves. More than 30 years ago, methods were developed for the inhalation of nebulized solutions of epinephrine, and this form of administration has proved to be a valuable aid in the treatment of bronchospastic disorders. Today, inhalation techniques have become an accepted part of the treatment program of many bronchopulmonary disorders.

Inhalation techniques have been developed to a high degree by anesthesiologists because of their interest in gases used for anesthesia and because of their desire to insure adequate airways for the postoperative period. Surgeons likewise share in the concern about the trachea and bronchi of the patient before and after operation. Chest physicians, allergists and pulmonary physiologists, however, have been more concerned with patients who have respiratory handicaps[1] of the kind treated non-

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surgically. All have had a hand in developing the principles and techniques of aerosol therapy.

Nearly all modern hospitals have facilities and equipment for inhalation therapy, and many have special departments devoted to treatment of this type. Technicians have been trained in the use of the equipment and the administration of therapeutic aerosols. In fact, a society of such technicians has been formed recently, The American Association of Inhalation Therapists. In addition, there is now an agency for the certification of well-trained technicians called The American Registry of Inhalation Therapists. Qualified technicians may take examinations under the auspices of the registry, and those who pass are given the degree or title of Registered Inhalation Therapist. This gives the inhalation therapist a certain status or recognition in his field, based on training, experience and dedication to his work.

Obviously, the work of these inhalation-therapy technicians must be supervised by competent and well informed physicians. For the most part, physicians who direct the activities of an inhalation-therapy department are specialists in anesthesiology or in thoracic medicine or surgery. Not only must such physicians recognize the indications for various types of inhalation therapy, they must be acquainted with the many mechanical devices that are available for inhalation therapy. In addition they must be well informed concerning the wide variety of medications and other substances that may be used in aerosol form for the treatment of bronchopulmonary disease. In fact, the physician must be in a position to evaluate critically the devices and the agents that are currently available for aerosol therapy. In particular, these physicians must not fall prey to the extravagant claims sometimes made by the makers of the mechanical devices or the substances to be nebulized. By the same token, the internist, the surgeon or the anesthesiologist who takes care of chest problems must be prepared to accept with reservation the pronouncements of some of our medical colleagues who have been enthusiastic proponents of inhalation therapy.

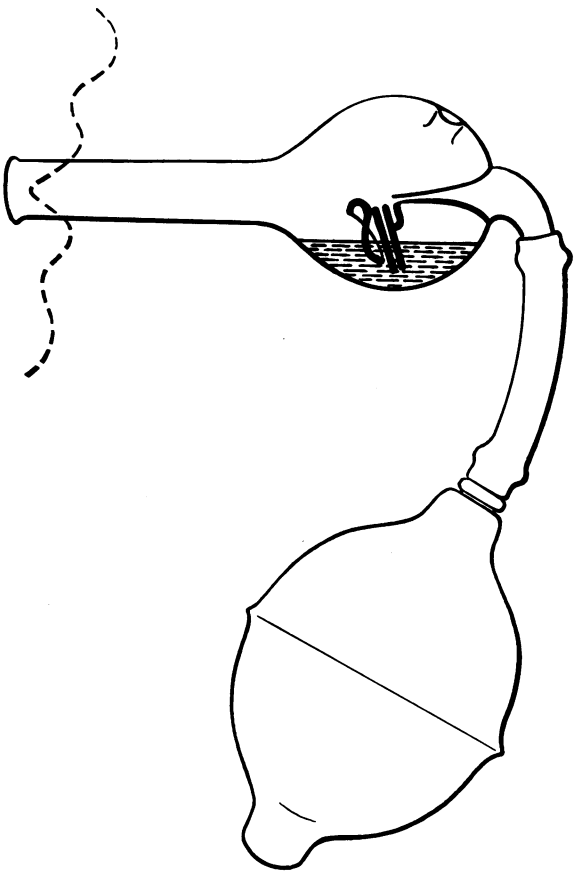

Figure 1.—Small-capacity nebulizer with hand bulb.

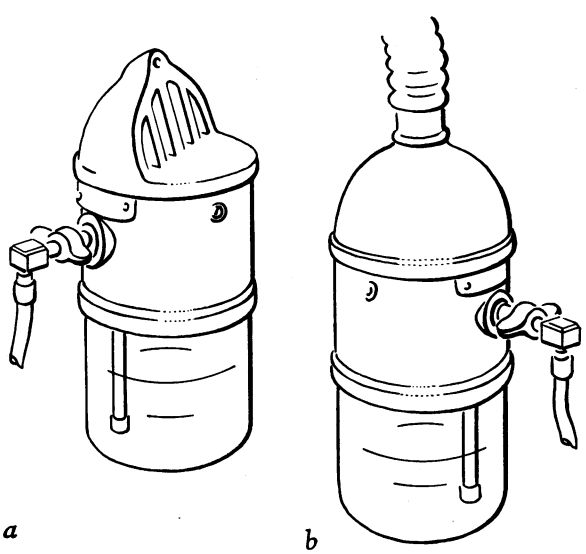

Figure 2.—Large-volume aerosol generator. (*a*) Open-type for tents and croupettes. (*b*) Closed type for use with face tents and masks.

PRODUCTION AND ADMINISTRATION OF AEROSOLS

Aerosol therapy has three principal objectives: Mobilization of bronchial secretions, relief of bronchospasm and topical chemotherapy. In order to achieve these objectives, proper equipment must be available and appropriate substances used for aerosolization. Usually, aerosols administered to the respiratory tract are mists created from liquids by atomizers or nebulizers. As a rule, the particles produced by atomizers are large and therefore tend to "fall out" of the air stream shortly after they are produced. Thus atomizers are used principally in the mouth and upper part of the respiratory tract. Properly constructed nebulizers, however, can make particles small enough to be carried by the air stream into the smaller bronchi or alveoli where the therapeutic effect is desired.[5] In general, the op-

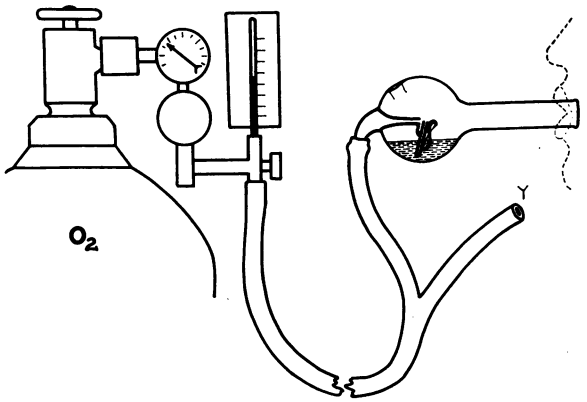

Figure 3.—Small nebulizer with Y-tube assembly in which the positive pressure is supplied by compressed oxygen. (Reprinted from Olsen, A. M.: Nebulization therapy in bronchiectasis: The use of penicillin and streptomycin aerosols, J.A.M.A., 134:947-952, July 1947.)

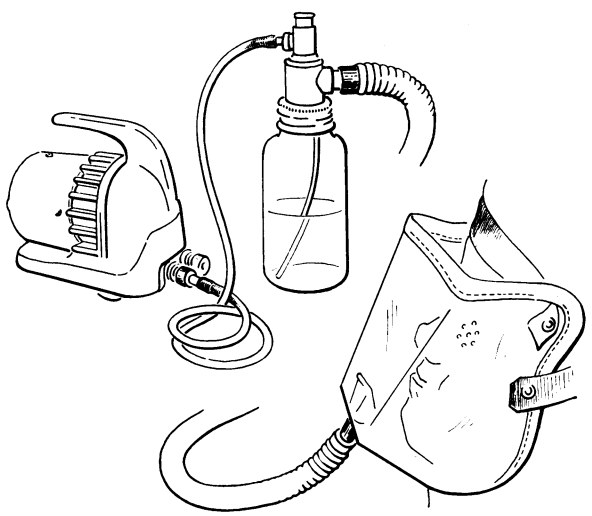

Figure 4.—Large-volume nebulizer deriving air pressure from motor-air compressor and delivering aerosol to face tent.

timal particle size for such nebulization is 0.5 to 2.5 micra.[6] Larger particles are deposited in the trachea or the major bronchi. The extremely small particles which are less than 0.5 micron in size not only pass into the alveoli but are also exhaled with the expired air. Dust aerosols do exist, but because of the large particle size and irritant effect in the bronchial tree, they have limited usefulness.

A number of nebulizers that are so constructed that most of the particles in the mist are optimal size are available. Some have small capacity for the administration of small amounts of medication at intervals (Figure 1). Others are big enough to permit giving aerosols continuously over a long period (Figure 2).

To produce the mist, a source of positive pressure is necessary. This may be supplied by compressed air or oxygen, or by a small motor air

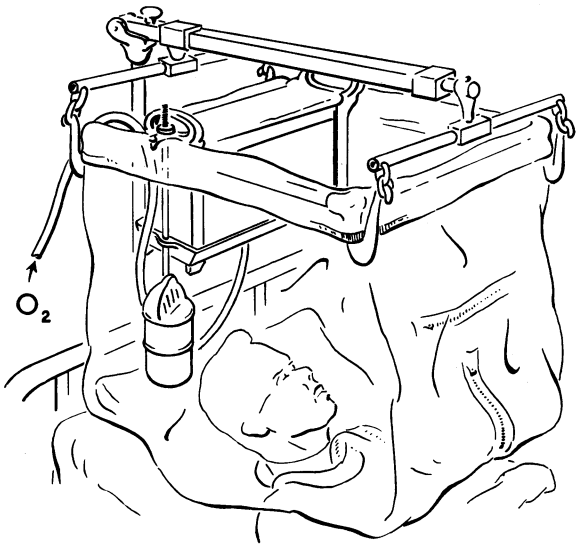

Figure 5.—Large-volume generator delivering aerosol to tent.

compressor. For the administration of a small amount of aerosol, a hand bulb using the small standard nebulizer may be sufficient. When the small nebulizer is operated with a motor-powered air compressor or oxygen, a Y-tube assembly will make it possible to provide the aerosol only during the inspiratory phase of inspiration, thus saving a good deal of the medication (Figure 3).

The aerosol may be delivered from the nebulizer to the patient in a variety of ways. As already indicated, the nebulizer itself may be placed in the mouth. However, a small nebulizer can deliver the aerosol to a mask. With the large generator, aerosols can be delivered via rubber or plastic tubing to a face tent (Figure 4) or to a tent designed for aerosol therapy (Figure 5). Likewise, the aerosols can be delivered to a unit that delivers oxygen or air to the patient with intermittent positive pressure (Figure 6). Nebulizers are now available that will pre-heat the aerosol so that it is delivered to the patient at a temperature of 90° to 125° F. Special attachments are available for introducing aerosols through tracheal tubes (Figure 7).

In general, the amount of aerosols delivered to the patient is greater when the nebulizer is close to him and is less when the aerosol has to be passed through a great deal of tubing. If the tubing is necessary, it should be of wide diameter.

AEROSOLS USED IN INHALATION THERAPY

Humidification and Liquefaction of Bronchopulmonary Secretions

In order to keep the normal mucous membranes of the respiratory tract in a healthy state, humidity of more than 40 per cent is desirable. Although

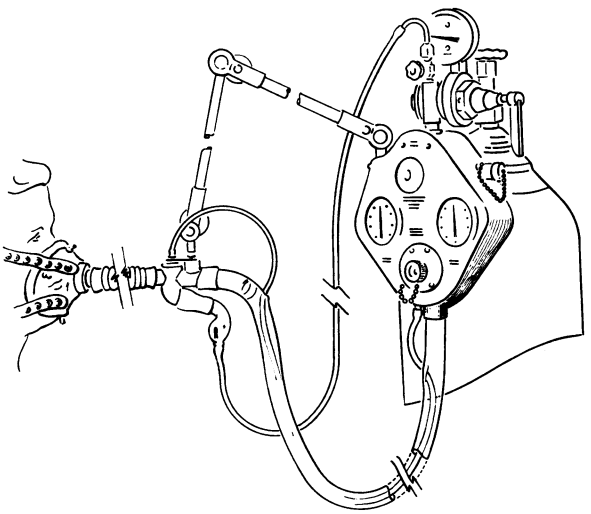

Figure 6.—Small nebulizer delivering a bronchodilator as in aerosol form to flow-sensitive positive-pressure unit (side-stream nebulization).

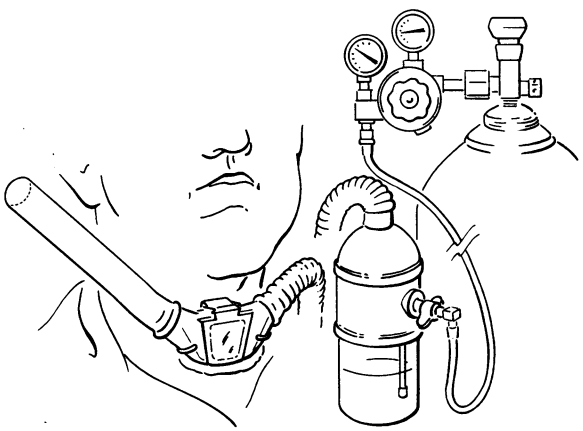

Figure 7.—Large-volume nebulizer delivering water aerosol to tracheal tube (main-stream nebulization).

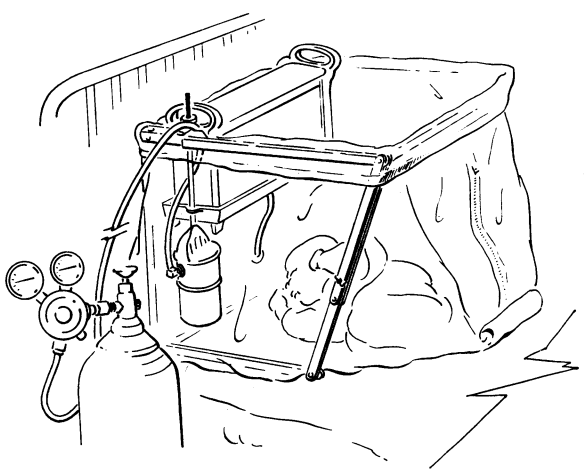

Figure 8.—Large-volume nebulizer delivering water aerosol to a croupette for treatment of tracheobronchitis in an infant.

seldom a problem to persons who live in warm climates, low humidity does become important in cold climates, especially in the winter months when artificial heating is necessary. Ordinary humidifying equipment is often woefully inadequate, and the dry air is certainly a factor in the frequency of respiratory infections. Adequate humidification is certainly an important factor in the prophylaxis of the common cold. The old-fashioned steam kettle served a useful purpose in its day and it still has value if used in relatively small, closed areas. In the home, electrically operated "cold steam" units are particularly valuable during the cold, dry winter months to supplement the humidifier attached to the furnace.

In the presence of respiratory disease, common humidifying devices are not sufficient for the liquefaction of viscous secretions retained in the bronchial tree, particularly because the large particles do not reach the smaller bronchi. Nebulizers capable of producing water vapor made of tiny particles are much more efficient in delivering the high humidity necessary for the liquefaction of secretions. Water or normal saline solution may be placed in large-volume nebulizers, and the mist delivered to ordinary bed tents, face tents, masks, nasal catheters, tracheal tubes or other devices. The addition of a "carrying agent" such as 10 per cent solution of propylene glycol may help in delivering the aerosol to the peripheral portions of the bronchial tree by inhibiting evaporation of the suspended water particles. The effectiveness of the mist can be augmented by pre-heating the aerosol in thermostatically controlled, large-volume nebulizers.[2] Warm aerosols are carried farther into the bronchial tree than cold aerosols before precipitation.

The most important agent for the liquefaction of secretions is water. Obviously, to be effective the water must be delivered to the smaller bronchi. The principal variables which determine the distribution of the water mist or any other aerosol to the bronchial tree include (1) the percentage saturation of inspired air, (2) the temperature of the aerosol, (3) the average particle size of the vapor and (4) the ability of the patient to ventilate.

The steam room formerly used by many hospitals in treatment of tracheobronchitis and pneumonia in children used a warm, completely saturated water vapor. The particle size was ignored and the needs of infants for oxygen or assisted respiration were not met. Furthermore, the steam room was most uncomfortable for the patient and the attendants who, incidentally, could hardly see the patient. A great advance in therapy took place when it

became possible to introduce micronized water vapor into a small tent or croupette (Figure 8). Either compressed air or compressed oxygen could be used to operate the nebulizer. With the modern croupette, tracheostomy is rarely necessary unless it is needed for the aspiration of secretions or for the attachment of a device to assist respiration.

Oxygen has been a valuable aid in the treatment of pneumonia and other conditions that may cause hypoxia. Oxygen, however, is extremely dry even though it has been bubbled through a water bottle. Administration of "dry" oxygen may result in the thickening of bronchopulmonary secretions, thus adding the factor of bronchial obstruction to the problems of a sick patient. Now it is possible to saturate oxygen with micronized water mist by putting the nebulizer in the main stream of the oxygen flow (Figure 7). This may be accomplished with bed tents, face tents, nasal catheters or masks.

Agents employed in the liquefaction of bronchial secretions are listed in Table 1.

When prolonged use of humidifying aerosols is desirable, normal saline solution may be preferable. Evidence suggests that the addition of sodium chloride may be helpful in the liquefaction of certain types of mucus. Because of this, half molar (2.9 per cent) solutions of saline have been employed in the treatment of mucoviscidosis.[3] Carrying agents such as glycerin or propylene glycol may also be used.

Other substances besides water and saline solution have been recommended to aid in the liquefaction process. These fall into two categories, namely, detergents and enzymes. Undoubtedly, the detergents such as tyloxypal do aid in the mobilization of secretions by decreasing the surface tension of the mucus and separating it from the bronchial walls. Likewise, enzymes have been employed because of their mucolytic action. The proteolytic enzyme, trypsin, digests protein matter in exudates, while pancreatic dornase acts by depolymerizing the desoxyribonucleic acid present in mucus.[9] Unfortunately, both the detergent and the enzyme preparations are themselves capable of causing enough irritation in the bronchial tree to produce bronchorrhea. Therefore, such substances should be used with discretion. The search for more satisfactory mucolytic agents continues. Improvement in techniques of delivering aerosols is still possible. Physicians must not lose sight of the great importance of oral and parenteral fluids in sputum liquefaction, or of the value of iodides and other expectorant agents.

TABLE 1.—*Liquefaction of Bronchial Secretions*

Water nebulization (humidification)
Hygroscopic agents
Aerosols of salt solution
Heated aerosols (tepid or superheated)
Inhalation of wetting agents and enzymes

Aerosols for Relief of Bronchospasm

The value of epinephrine derivatives administered by the aerosol method has long been recognized. Ordinarily, a small amount of the solution is placed in a small-capacity nebulizer, either of the glass or plastic type, and the patient delivers the bronchodilator with the aid of a hand bulb. Treatments for the relief of asthma are usually of very short duration and, therefore, only a few inhalations are required. Recently developed, small units which employ the gas phase of dichlorodifluoromethane as a propellant for the nebulization of the bronchodilator aerosol have proved to be satisfactory. As was previously noted, devices employing a bronchodilator prepared in powdered form have generally been less satisfactory.

Derivatives such as isoproterenol sulfate, isoproterenol hydrochloride, and racemic epinephrine have largely replaced epinephrine itself (1:100 solutions) in the treatment of bronchospasm. At times, medicaments containing vasoconstrictor, antihistaminic or anticholinergic drugs or steroids have been nebulized alone or in combination with epinephrine aerosols. Such preparations have a limited value in the management of bronchospastic disorders.

Chemotherapeutic and Antibiotic Aerosols

When penicillin and other antibiotics became available, it was hoped that the aerosol method would be the preferred route of administration in bronchopulmonary disease. I was among the most enthusiastic about the possibilities at that time.[7] Certainly, the initial results of penicillin aerosol therapy in bronchiectasis were most encouraging. Both penicillin and streptomycin were well tolerated in aerosol form by the tracheobronchial tree. In time, however, an increasing number of patients became sensitive to these antibiotics, especially to penicillin. Other antibiotics of the broad-spectrum type have never been very satisfactory because they often produce local irritation in the bronchial tree. When the various antibiotics were administered by the aerosol technique, the effect appeared to be topical in nature, although penicillin was absorbed as was demonstrated by significant concentrations of penicillin in the blood stream.

Even more disturbing than the allergic reactions to penicillin and other drugs was the emergence of resistant strains of bacteria in the bronchopulmonary secretion. At present, significant organisms recovered from tracheobronchial secretions are rarely sensitive to penicillin. Furthermore, prac-

TABLE 2.—*Antibiotics by Aerosol: Dosage Schedule**

Drug	Dose per cc. of Water or Saline	Drug	Dose per cc. of Water or Saline
Penicillin	50,000 units	Neomycin	200 mg.
Streptomycin	200 mg.	Polymyxin	10 mg.
Tetracycline	125 mg.	Novobiocin	250 mg.
Chloramphenicol	250 mg.	Kanamycin	250 mg.

*Usually administered 2 cc. four times daily.

tically all of the antibiotics can be administered orally or parenterally with just as satisfactory results as the results from administration of the drugs by aerosol. This does not mean, however, that the aerosol method has been discarded in the management of bronchitis, bronchiectasis, lung abscess, mucoviscidosis, certain pneumonias, bronchospasm and other pulmonary affections. On the contrary, the beneficial effects of the aerosol techniques in the liquefaction of secretions and relief of bronchospasm are more clearly recognized than ever. I suspect that in a large part our early favorable results with chemotherapeutic aerosols could be attributed to the sputum liquefaction effect.

There are, of course, certain antibiotic preparations which are toxic when given by parenteral means and which may be very effective on aerosolization. As early as 1941, glucosulfone (Promin®) and other sulfonamides were administered by aerosol for tracheobronchial disease and proved to be effective. Today, we may use neomycin or polymyxin or other drugs by nebulization when the bronchopulmonary secretions contain organisms resistant to the usual antibiotics but sensitive to one of these more toxic drugs (Table 2).

INDICATIONS FOR AEROSOL THERAPY

As has already been stated, the inhalation of aerosols is indicated for the liquefaction and mobilization of secretions, the relief of bronchospasm, the topical administration of antibiotics to the tracheobronchial tree and at times for the suppression of turbulence in bronchopulmonary secretions. At times, aerosols may be used which combine the therapeutic effects of humidifying, bronchodilating and antimicrobial agents. The method of administering the aerosol will also vary with the circumstances.

Aerosols may be used in a wide variety of respiratory problems. Water aerosols have been employed for the principal purpose of liquefying secretions in other conditions besides the infectious tracheobronchitis of infants and the pneumonias of children or adults. For example, after removal of foreign bodies from the bronchi in children, use of aerosol mist in a croupette or tent for a day or two is almost always desirable. Water or normal saline solution in aerosol form may help in the resolution of the tracheobronchitis that often follows severe upper respiratory infections or influenza.

Inhalation therapy has been helpful in the preoperative preparation and postoperative care of surgical patients. Patients with asthma, asthmatic bronchitis, emphysema, smokers' cough or bronchiectasis should receive preoperative preparation for a time. The type of aerosol used will vary according to the patient's problem. Water or saline solution may be given by face tent for 15 to 30 minutes of every hour. Ten to twenty drops of isoproterenol (1:400) may be given by a small nebulizer and Y tube four times daily. Sometimes it is desirable in preoperative preparation to use a positive pressure machine to deliver the bronchodilator so that the patient will be familiar with the method in the event that it is needed in the postoperative period.

All postoperative patients with bronchopulmonary disorders should receive humidifying aerosols several times a day. When bronchodilating drugs are necessary in the postoperative period, the intermittent positive-pressure-breathing technique is often an excellent method of administration. In the presence of tenacious secretions, careful use of tyloxypal preparations or pancreatic dornase (50,000 units per cubic centimeter) is justified if the secretions cannot be raised with the help of water or saline aerosols. These substances are best given by the nebulizer-Y tube technique or with the positive pressure unit and usually are administered four times daily.

Use of humidifying aerosols is imperative for patients with tracheotomy, especially after surgical procedures. Very satisfactory devices are available for the administration of aerosol-oxygen mixtures to tracheotomy tubes (Figure 7), and flow-sensitive or piston-type pressure respirators can be attached to the tracheal tubes.

Patients with poliomyelitis, paraplegia or other diseases of the nervous system and those with generalized muscular diseases are often candidates for aerosol therapy. Early and frequent use of humidifying aerosols may keep these patients out of trouble. Often these patients need assistance to respiration such as tank or chest respirators or cycling devices attached to tracheostomy tubes. The cough machine is of value for this group of patients.

Antibiotic aerosols may be added to the care of any of these patients if susceptible organisms are isolated from the sputum or bronchial secretion. The aerosol route is especially indicated if oral

or parenteral administration of the antibiotic is contraindicated. This may be the case with neomycin, polymyxin, kanamycin, streptomycin and chloramphenicol, the systemic absorption of which is often undesirable (Table 2).

Patients with pulmonary emphysema often have associated bronchospasm, bronchitis and retention of viscous secretions. The presence or absence of bronchospasm in these cases can easily be demonstrated by a measurement of the vital capacity and maximal breathing capacity before and after use of a bronchodilator. If bronchospasm complicates pulmonary emphysema, measures should be taken to relieve the bronchospasm. These include elimination of all respiratory irritants, including tobacco smoke, and trial of orally administered bronchodilators. Usually too, systematic administration of a measured amount of aerosol bronchodilator about four times a day is desirable.[4] Inasmuch as the patient must nebulize about 1 cc. of solution for each dose, the hand bulb technique is impractical. Most of these patients are able to nebulize the required amount of solution by using an ordinary glass or plastic nebulizer connected to an oxygen or a motor-air compressor with a Y tube incorporated into the system (Figure 3). Occasionally a mask or a rebreathing bag of some type may be desirable. To some patients, the bronchodilator aerosol is administered more efficiently with the aid of an intermittent positive pressure device that uses the patient's own breathing effort to trip a valve, which permits a forced flow of oxygen or air under pressure to enter the tracheobronchial tree. For most patients with emphysema this apparatus is valuable only when it does a more effective job of delivering the bronchodilator to the bronchial tree.

Intermittent positive pressure breathing may provide for more adequate ventilation of the bronchial tree during the time that the machine is in operation.[8] For a short time, the distribution of the inspired air to portions of the lung which are poorly ventilated may be improved. It is questionable, however, whether the benefits of the temporary hyperventilation of the lung persist for any appreciable period after intermittent positive pressure breathing is discontinued. Thus, the value of using intermittent positive pressure breathing routinely in all cases of emphysema is seriously questioned. However, in patients with respiratory acidosis caused by retention of carbon dioxide, frequent, more continuous use certainly may improve pulmonary ventilation and thus may eliminate carbon dioxide, reduce hypoxia and help in restoring the normal chemical composition of the blood.

The use of a volatile alcohol by inhalation has proved to be very beneficial as an antifoaming agent in the treatment of pulmonary edema, and the administration by nebulizer of defoaming agents containing silicone is likewise helpful in suppressing the secretions of pulmonary edema. By the same token, positive pressure respiration alone may be helpful in combatting this condition, especially when it is combined with other methods of treating the acutely edematous lung.

Much credit must be given to the manufacturers of the various nebulizers, tents, masks, positive-pressure machines and cough machines. Many of these pieces of apparatus are ingenious, well made and most useful. Similarly, the various pharmaceutical houses must be commended for providing the medical profession with a variety of substances and solutions which are useful when administered with the previously mentioned equipment. It is natural that these manufacturers should advertise their wares to the medical profession. It is the duty of the physician who is in charge of the patient, however, to evaluate critically the indications for therapeutic aerosol. Also, he should personally supervise the activities of the inhalation-therapy technicians, and he should acquaint himself with the mechanics of the various pieces of equipment so that he does not rely entirely on the judgment of the technician. Inhalation therapy, when indicated, must be prescribed individually for each patient by the physician, and under no circumstances should administration of positive pressure or any other type of therapy be made routine.

Every hospital today should have a training or instruction program in aerosol-therapy techniques for those members of the staff who are directly concerned. This includes all members of the department of anesthesia, all surgeons, all internists and chest specialists who are involved in the care of patients with pulmonary and bronchial diseases. It is particularly important that the house staff in every hospital be thoroughly trained in the use of such equipment and instructed in the indications for the various types of aerosols.

Likewise, the nursing staff should be acquainted with the operation of oxygen equipment, nebulizers, positive-pressure machines and respirators. Failure of the nursing staff to understand the operation of the equipment might prove fatal. In any case, the operation of the various devices and the administration of aerosols must not be left entirely to the oxygen-therapy technician. Valuable as such technicians are, they do not have the special knowledge and training in medicine essential for the treatment of disease. If therapeutic aerosols are to be used properly and intelligently, the medical profession must assume full responsibility for the administration.

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